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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,271	01/04/2006	Hui-Fang Chang	101151-1P US	6300

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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,271	CHANG ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-17 and 22* is/are allowed.

6)☒ Claim(s) *18,21,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's amendment and remarks submitted February 20, 2008 wherein claims 18 and 24 are amended and claims 19, 20, 25, and 26 are cancelled. This application is a national stage application of PCT/GB04/02904, filed July 6, 2004, which claims benefit of provisional application 60/485523, filed July 8, 2003.

Claims 1-18 and 21-24 are pending in this application.

Claims 1-18 and 21-24 as amended are examined on the merits herein.

Applicant's arguments, submitted February 20, 008, with respect to the rejection of instant claims 1-14 under 35 USC 103(a) for being obvious over Katayama et al., have been fully considered and found to be persuasive to remove the rejection as further consideration has determined that one of ordinary skill in the art would not have made the specific compounds of the instant claims based on the disclosure of Katayama et al. Therefore the rejection is withdrawn.

Applicant's arguments, submitted February 20, 008, with respect to the rejection of instant claims 15-17 under 35 USC 103(a) for being obvious over Katayama et al. in view of Holladay et al. in view of Bylund et al., have been fully considered and found to be persuasive to remove the rejection as further consideration has determined that one of ordinary skill in the art would not have made the specific compounds of the instant claims based on the disclosure of Katayama et al. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, for failing to comply with the enablement requirement. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. "Prevention" as discussed herein is interpreted to mean the complete blocking of all symptoms or effects of a disorder for an indefinite period of time.

Nature of the invention: The claimed invention is drawn to a therapeutic method for treatment or prevention of a disorder. According to Merriam-Webster's Collegiate

Dictionary, Tenth Edition, the word "prevent" is defined as, "to deprive of power or hope of acting or succeeding; to keep from happening or existing." The word "prophylactic," is defined as "guarding from or **preventing** disease," and the word "prophylaxis," is defined as, "measures designed to preserve health and **prevent** the spread of disease." In order for a preventative method to truly deprive a condition of power or hope of acting or succeeding, the treatment must be 100% successful at avoiding any occurrence of said condition at any time in the future.

The state of the prior art: The nicotinic acetylcholine receptor is known in the prior art to be involved in certain neurological disorders such as for example Alzheimer's disease. Ligands to this receptor have been used as therapeutic agents. These ligands are not known to be useful as preventative agents in the sense being used herein. In general, prevention of any disorder in the sense being used herein is not a recognized clinical outcome in the art, as no treatment is perfectly effective.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: Prevention of a disease is not the same as treatment of said disease. In order to prevent a disease, as opposed to merely delaying or reducing its symptoms, a treatment must either render the subject completely resistant to said disease after a single treatment or a limited number of treatments, or else, when continued indefinitely, continue to completely suppress the occurrence of said disease. In order to practice a preventative method, one of skill in the art must know the answer to several questions in addition to the effectiveness of the therapy in short-term relief of symptoms, including:

1) What is the duration of a single course of therapy? How often must the therapy be administered to completely suppress the disease?

2) Does the subject develop tolerance to the therapy over time? Does the disease eventually progress to a point where the therapy is unable to completely suppress all symptoms? For example, will a metastatic cancer eventually adapt to overcome treatments directed to preventing it from metastasizing into the bone? Or will a case of osteoporosis or rheumatoid arthritis ultimately progress to a point where symptoms develop regardless of which therapy is administered.

3) What are the long-term effects of the therapy? Does it cause progressive damage to the kidneys, liver, or other organs? Does the active agent accumulate in the subject's tissues? Is the minimum dose necessary to completely prevent the disease safe for long-term administration? Are there any steps that can be taken to reduce side effects?

For this reason, many therapies which are suitable for short-term relief of symptoms are not suitable for lifelong prevention of disease. For example, antibiotics, chemotherapeutics, and antiviral drugs are not normally administered to healthy subjects in order to prevent the development of infection or cancer.

The Breadth of the claims: In the absence of an explicit definition in Applicant's specification, the claims are given their broadest reasonable interpretation. See MPEP 2111. As discussed above, prevention in the sense used herein must be capable of stopping any occurrence of a condition at any time in the future. Merely slowing the

onset of disease or making the disease less likely would still leave it with "power or hope of acting or succeeding," and thus not qualify as prevention.

The amount of direction or guidance presented: The claimed compounds are shown to be ligands for the nicotinic acetylcholine receptor, which suggests a **therapeutic** utility. No guidance is given in the specification suggesting any reason to believe that the claimed compounds are uniquely useful as preventative agents.

The presence or absence of working examples: No working examples for the prevention or prophylaxis of disease are provided.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the prevention of disease. See MPEP 2164.

The quantity of experimentation necessary: As mentioned above, the short-term usefulness of a therapy for relief of symptoms is no guarantee of its long-term usefulness for prevention of disease. Because no guidance is given for the use of the claimed therapeutic method for the long-term prevention of disease, one skilled in the art wishing to practice the invention would be unable to do so without first gathering information as to the long-term effectiveness of the therapy. In particular, one skilled in the art, in order to practice the invention for prevention of disease, would need to know whether the preventative effect remains potent over the long term.

In order to answer these questions in the absence of any existing data, one skilled in the art, in order to practice the invention, would undertake long-term animal

tests, preferably over a period of years, preferably involving a relatively long-lived experimental animal such as dogs or monkeys, or a human clinical trial. Animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Administering the claimed compounds for a period of years to a suitable subject population is an undue amount of experimentation needed in order to practice the full range of the claimed invention. As prevention in the full sense is an extremely high bar for any clinical outcome, there is no reason to believe that the therapy would be successful, and any actual success would be a surprising and unpredictable result.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the nature of the invention, Applicants fail to provide information sufficient to practice the claimed invention for the prevention of a disorder associated with the nicotinic acetylcholine receptor.

Response to Argument: Applicant's arguments, submitted February 20, 2008, with respect to the above ground of rejection, have been fully considered and not found

to be persuasive to remove the rejection. Applicant argues that the claims have been amended to overcome the rejection by removing the word, "prophylaxis" from the claims. However, he rejection was additionally also based on the appearance of the term "preventing" in claim 23. As claim 23 is still drawn to a method of preventing, the rejection still stands as regards this claim. Therefore the rejection is deemed proper and made **FINAL**.

Claims 18, 21, 23, and 24 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method of treating a "human disease or condition in which activation of the α7 nicotinic receptor is beneficial." In order to practice a method for a broad class of embodiments, one skilled in the art must

be able to reasonably and exhaustively define which disorders are included within the claim limitations.

The state of the prior art: Nicotinic acetylcholine receptors are suspected to be involved in certain neurological disorders such as for example Alzheimer's disease. However, there are multiple subtypes of this receptor, with differing biological activities. According to Holladay et al. (Reference included with previous office action) the role of the α7 nicotinic acetylcholine receptor is still under investigation. Therefore it is not known what if any disorders can be treated by agonists of this receptor. Furthermore, the prior art does not exhaustively disclose a complete explanation of the causes of every neurological disorder, in such a way as to reveal to one skilled in the art all disorders affected by said receptor.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The study of neurological disorders is highly unpredictable. One skilled in the art would not know for certain the full range of neurological and psychiatric effects of α7 nicotinic receptor activation, or the exact biochemical causes of each and every neurological disorder. Often, neurological disorders are known by symptoms (e.g. psychosis, intellectual impairment) rather than as being related to a specific biochemical cause.

The Breadth of the claims: The claimed invention is very broad, including any disorder that can be improved by activation of a particular receptor. Dependent claims 19 and 25 limit the claimed disorders to neurological disorders, psychotic disorders, and

intellectual impairment disorders. Neurological disorders include any disorder related to the physiological function of the brain. Psychotic and intellectual impairment disorders are defined by certain general types of symptoms without regard to the underlying symptoms, if such are even known. Claim 21 includes treatment of pain, which is a broad class of disorders including pain arising from nociceptive stimuli, neuropathic disorders ,and psychogenic conditions.

While members of a particular class of receptors share certain similarities, there is no expectation that they will produce the same biological effects or be useful for treating the same disorders. It is highly unpredictable which members of a receptor family will be useful for treating which disorders.

The amount of direction or guidance presented: The only direction or guidance presented is the indication that the claimed compounds activate the α7 nicotinic receptor, and are thus expected to possess similar utility to prior art compounds that activate the same receptor. However, the prior art does not actually provide enabling disclosure of therapeutic methods using similar compounds. No new information as to the therapeutic utility of this class of receptor ligands is provided.

The presence or absence of working examples: No working examples are given for the treatment of any disorder whatsoever.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the treatment of broad classes of neurological disorders. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the claimed invention, one skilled in the art would need to know which disorders are in fact treatable by the claimed method. Because of the incomplete knowledge in the art and the lack of further guidance or examples from Applicant's specification, one skilled in the art would have to independently determine the full scope of disorders that can be treated by the disclosed therapy. In fact there is no conclusive reason to believe that these compounds can be used to treat any disorders. Finding clinical indications for these compounds would require extensive investigation, both theoretical and experimental, of numerous neurological and psychological disorders, as well as the biochemical systems involved, and would require further research on the biological function of the α7 receptor. Such original experimentation is neither routine nor predictable, and therefore constitutes an undue burden of unpredictable research.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the lack of guidance or working examples, Applicants fail to provide information sufficient to treat a disorder with an agonist of the α7 nicotinic receptor.

Response to Argument: Applicant's arguments, submitted February 20, 2008, with respect to the above ground of rejection, have been fully considered and not found

to be persuasive to remove the rejection. Applicant argues that the claims have been amended to recite specific, limited classes of disorders which are associated with reduced cholinergic function and can be mediated through the action or nicotinic acetylcholine receptors. Firstly, claim 23 has not been amended and is still drawn to a broad, functionally defined class of disorders. Therefore the rejection of this claim remains. Secondly, the "specific diseases, disorders, and conditions," that have been added to limit the claimed subject matter include broad, vague, functionally defined classes of diseases such as learning deficits, cognition deficits, attention deficit, memory loss, neurodegenerative disorders, anxiety, pain, and craving, all of which are functionally defined classes of pathology that do not share a common cause or treatment. For example, pain can be caused by tissue damage, nerve injury, phantom limb pain, postherpetic neuralgia, diabetic neuropathy, fibromyalgia, or complex regional pain syndrome, to name a few examples of pathological pain. Cognitive deficits, learning deficits, and memory loss can be caused by developmental disorders including chromosomal abnormalities such as Down's syndrome or fragile X syndrome, exposure to drugs or toxins, infection with pathogenic agents such as HIV, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jacob disease, or amoyotrophic Lateral Sclerosis, brain tumors, brain damage, stroke, or severe anoxia or malnutrition, for example. It is not expected based on the state of the art that these diverse conditions can be treated by modulating the nicotinic acetylcholine receptor. There is no way that one skilled in the art could treat all of the recited disorders by

administering a nicotinic acetylcholine receptor agonist. Thus the amendment is not seen to overcome the rejection.

Therefore the rejection is deemed proper and made **FINAL**.

Conclusion

Claims 18, 21, 23, and 24 are rejected. Claims 1-17 and 22 are seen to be allowable. Reasons for indication of allowable subject matter are as follows:

The claimed compounds and methods of assaying said compounds are seen to be adequately described and enabled by Applicant's specification. Specifically, p. 1 lines 9-21 provide adequate support for using nicotinic acetylcholine agonists as therapeutic agents. pp. 1-9 provide written description for the claimed compounds. Pp. 14-22 provide synthetic methods that enable one skilled in the art to make these compounds. Therefore the claims satisfy the requirements of 35 USC 112.

Furthermore the claims are seen to e novel and non-obvious over the prior art. The prior art does not disclose any compounds having the claimed spiro-azabicyclo-oxizolidinone compounds with two aryl groups attached to the oxazolidinone as recited in the instant claims. Although Katayama et al. discloses similar compounds having one substituted aryl group, this reference does not disclose compounds in which the aryl group is substituted with a second aryl group. One of ordinary skill in the art would not have had any motivation to modify these prior art compounds by adding an aryl substituent as shown in the instant claims.

For these reasons the indicated claims are seen to be allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
5/27/2008

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623